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☐	L6	(fgf adj 8 or fibroblast adj growth adj factor adj 8) and bone	2
☐	L5	(fgf adj 8a or fibroblast adj growth adj factor adj 8a) and bone	0
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FILE 'MEDLINE' ENTERED AT 14:46:39 ON 06 OCT 2006

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FILE 'BIOSIS' ENTERED AT 14:46:39 ON 06 OCT 2006

FILE 'CAPLUS' ENTERED AT 14:46:39 ON 06 OCT 2006

=> S FGF(W)8 AND BONE
L1 150 FGF(W) 8 AND BONE

=> dup rem l1
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L2 93 DUP REM L1 (57 DUPLICATES REMOVED)

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L2 ANSWER 80 OF 93 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:342359 BIOSIS
DOCUMENT NUMBER: PREV199900342359
TITLE: Genomic structure, mapping, activity and expression of fibroblast growth factor 17.
AUTHOR(S): Xu, Jingsong; Lawshe, Avril; MacArthur, Craig A.; Ornitz, David M. [Reprint author]
CORPORATE SOURCE: Department of Molecular Biology and Pharmacology, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Mechanisms of Development, (May, 1999) Vol. 83, No. 1-2, pp. 165-178. print.
CODEN: MEDVE6. ISSN: 0925-4773.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Aug 1999
Last Updated on STN: 24 Aug 1999

AB Fibroblast growth factors are essential molecules for development. Here we characterize Fgf17, a new member of the fibroblast growth factor (FGF) family. The Fgf17 gene maps to mouse chromosome 14 and is highly conserved between mouse and human (93% identity). It exhibits 60% amino acid identity with Fgf8 and 50% identity with Fgf18. Both Fgf8 and Fgf17 have a similar structure and a similar pattern of alternative splicing in the 5' coding region. When expressed in 3T3 fibroblasts, mouse FGF17 is transforming, indicating that it can activate the 'c' splice form of either FGF receptor (FGFR) one or two. During midgestation embryogenesis, in situ hybridization analysis localized Fgf17 expression to specific sites in the midline structures of the forebrain, the midbrain-hindbrain junction, the developing skeleton and in developing arteries. Comparison to Fgf8 revealed a striking similarity in expression patterns, especially in the central nervous system (CNS), suggesting that bothgenes may be important for CNS development, although Fgf17 is expressed somewhat later than Fgf8. In the developing skeleton, both genes are expressed in costal

cartilage while Fgf8 is preferentially expressed in long bones. In the developing great vessels Fgf17 is preferentially expressed, suggesting that it may have a more prominent role in vascular growth.

L2 ANSWER 81 OF 93 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 1999264281 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10330489
TITLE: Abnormal anteroposterior and dorsoventral patterning of the limb bud in the absence of retinoids.
AUTHOR: Stratford T; Logan C; Zile M; Maden M
CORPORATE SOURCE: Developmental Biology Research Centre, Biomedical Sciences Division, King's College London, London, UK.
SOURCE: Mechanisms of development, (1999 Mar) Vol. 81, No. 1-2, pp. 115-25.
Journal code: 9101218. ISSN: 0925-4773.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 30 Jul 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 20 Jul 1999

AB We describe here how the early limb bud of the quail embryo develops in the absence of retinoids, including retinoic acid. Retinoid-deficient embryos develop to about stage 20/21, thus allowing patterns of early gene activity in the limb bud to be readily examined. Genes representing different aspects of limb polarity were analysed. Concerning the anteroposterior axis, Hoxb-8 was up-regulated and its border was shifted anteriorly whereas shh and the mesodermal expression of bmp-2 were down-regulated in the absence of retinoids. Concerning the apical ectodermal genes, fgf-4 was down-regulated whereas fgf-8 and the ectodermal domain of bmp-2 were unaffected. Genes involved in dorsoventral polarity were all disrupted. Wnt-7a, normally confined to the dorsal ectoderm, was ectopically expressed in the ventral ectoderm and the corresponding dorsal mesodermal gene Lmx-1 spread into the ventral mesoderm. En-1 was partially or completely absent from the ventral ectoderm. These dorsoventral patterns of expression resemble those seen in En-1 knockout mouse limb buds. Overall, the patterns of gene expression are also similar to the Japanese limbless mutant. These experiments demonstrate that the retinoid-deficient embryo is a valuable tool for dissecting pathways of gene activity in the limb bud and reveal for the first time a role for retinoic acid in the organisation of the dorsoventral axis.

L2 ANSWER 82 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:251271 CAPLUS
DOCUMENT NUMBER: 128:304811
TITLE: Cloning and cDNA sequence of human fibroblast growth factor homologous factor zFGF-5
INVENTOR(S): Deisher, Theresa A.; Conklin, Darrell C.; Raymond, Fenella C.; Bukowski, Thomas R.; Holderman, Susan D.; Hansen, Brigit; Sheppard, Paul O.
PATENT ASSIGNEE(S): Zymogenetics, Inc., USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9816644	A1	19980423	WO 1997-US18635	19971016

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2269083	AA	19980423	CA 1997-2269083	19971016
AU 9747583	A1	19980511	AU 1997-47583	19971016
AU 725551	B2	20001012		
EP 931148	A1	19990728	EP 1997-910128	19971016
EP 931148	B1	20060301		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9712348	A	19990831	BR 1997-12348	19971016
CN 1247568	A	20000315	CN 1997-199827	19971016
CN 1127568	B	20031112		
JP 2001502178	T2	20010220	JP 1998-518577	19971016
EP 1632574	A1	20060308	EP 2005-21714	19971016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 318906	E	20060315	AT 1997-910128	19971016
PT 931148	T	20060630	PT 1997-910128	19971016
ES 2258788	T3	20060901	ES 1997-910128	19971016
NO 9901796	A	19990616	NO 1999-1796	19990415
MX 9903530	A	20000131	MX 1999-3530	19990415
KR 2000049207	A	20000725	KR 1999-703306	19990416
PRIORITY APPLN. INFO.:			US 1996-28646P P	19961016
			EP 1997-910128 A3	19971016
			WO 1997-US18635 W	19971016

AB A novel DNA sequence is provided that encodes a fibroblast growth factor (FGF) homolog polypeptide having homol. to FGF-8. Anal. of the tissue distribution of the mRNA corresponding to this novel DNA showed that expression was highest in fetal and adult heart tissue, followed by apparent but decreased expression levels in fetal lung, skeletal muscle, smooth muscle tissues such as small intestine, colon, and trachea. The FGF homolog polypeptide is designated zFGF-5. The polypeptides, and polynucleotides encoding them, are proliferative for muscle cells and may be used for remodelling cardiac tissue and improving cardiac function. The present invention also includes antibodies to the zFGF-5 polypeptides.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 83 OF 93 MEDLINE on STN DUPLICATE 20

ACCESSION NUMBER: 1999144014 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9990203
TITLE: Signaling molecules involved in induction and early patterning of limb buds.
AUTHOR: Kawakami Y; Nohno T
CORPORATE SOURCE: Department of Molecular Biology, Kawasaki Medical School, Kurashiki, Japan.
SOURCE: Kaibogaku zasshi. Journal of anatomy, (1998 Dec) Vol. 73, No. 6, pp. 655-66. Ref: 97
Journal code: 0413526. ISSN: 0022-7722.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 20 Apr 1999
Last Updated on STN: 20 Apr 1999
Entered Medline: 7 Apr 1999

AB Soluble signaling factors are involved in morphogenetic events during vertebrate limb development. They belong to the Hedgehog family, the bone morphogenetic protein (BMP) family, the fibroblast growth factor (FGF) family and the Wnt family. FGF-8 and FGF-10 play central roles to specify the limb field and promote initial outgrowth. In the established limb bud, FGF-4, FGF-8 and BMP-2 are secreted in the apical ectodermal ridge and control proximal-distal pattern formation. In the zone of polarizing activity Sonic hedgehog is produced and pattern along the anterior-posterior axis. Members of the BMP family may be the secondary signals in this patterning. Wnt-7a from the dorsal ectoderm dorsalizes limb mesenchyme and controls dorsal-ventral patterning. These factors expressed in the signaling centers in limb buds influence gene expression each other and coordinate limb morphogenesis.

L2 ANSWER 84 OF 93 MEDLINE on STN
ACCESSION NUMBER: 1998264591 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9603428
TITLE: Fate map of the developing chick face: analysis of expansion of facial primordia and establishment of the primary palate.
AUTHOR: McGonnell I M; Clarke J D; Tickle C
CORPORATE SOURCE: Department of Anatomy and Developmental Biology, University College London, United Kingdom.. I.McGonnell@ucl.ac.uk
SOURCE: Developmental dynamics : an official publication of the American Association of Anatomists, (1998 May) Vol. 212, No. 1, pp. 102-18.
Journal code: 9201927. ISSN: 1058-8388.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 16 Jul 1998
Last Updated on STN: 16 Jul 1998
Entered Medline: 8 Jul 1998

AB Developing facial primordia change shape substantially in stages leading up to primary palate formation. We investigated expansion of cell populations within each of the four facial primordia of chick embryos between HH-stages 20 and 28, by using DiI labelling. Populations of cells centred around the nasal pits in the upper face, the midline of the paired mandibular primordia in the lower face, and at sites of fusion contribute most to overall expansion. Abundant Msx-1 transcripts are found in regions of high expansion, and Fgf-8 transcripts are seen in ectoderm associated with some of these regions. Many cell populations display preferential expansion along one axis. Maxillary and mandibular primordia cell populations expand along the proximodistal axis, whereas at the distal tip of the frontonasal mass, cell populations expand mediolaterally. Thus outgrowth occurs at the tips of mandibular and maxillary primordia, but at the base of the frontonasal mass. At regions where adjacent primordia abut each other, we found bidirectional movement of cells between primordia, unidirectional movement or could detect no movement at all. Regions of highest expansion in each primordium have the highest percentage of S phase labelled cells. Cell death occurs in some regions of low expansion but it seems likely that cell rearrangements and intercalations also contribute to shaping. These rearrangements could be associated with stretching of the primordia by neighbouring tissues. Treatment of chick embryos with retinoic acid causes clefts of the primary palate (Tamarin et al. [1984] J. Embryol. Exp. Morphol. 84:105-123). We found a decrease in expansion of cell populations that normally contribute to primary palate formation but surprisingly little ectopic cell death. Expansion of other cell populations in the treated upper face was more even rather than directed. This further supports the idea that tension exerted by neighbouring tissues plays a major role in global

shaping of the upper face.

L2 ANSWER 85 OF 93 MEDLINE on STN DUPLICATE 21
ACCESSION NUMBER: 1998197124 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9527879
TITLE: Morphological diversity of the avian foot is related with the pattern of msx gene expression in the developing autopod.
AUTHOR: Ganan Y; Macias D; Basco R D; Merino R; Hurle J M
CORPORATE SOURCE: Departamento de Ciencias Morfologicas y Biologia Animal y Celular, Universidad de Extremadura, Badajoz, 06071, Spain.
SOURCE: Developmental biology, (1998 Apr 1) Vol. 196, No. 1, pp. 33-41.
Journal code: 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 20 May 1998
Last Updated on STN: 20 May 1998
Entered Medline: 14 May 1998

AB The formation of the digits in amniota embryos is accompanied by apoptotic cell death of the interdigital mesoderm triggered through BMP signaling. Differences in the intensity of this apoptotic process account for the establishment of the different morphological types of feet observed in amniota (i.e., free-digits, webbed digits, lobulated digits). The molecular basis accounting for the differential pattern of interdigital cell death remains uncertain since the reduction of cell death in species with webbed digits is not accompanied by a parallel reduction in the pattern of expression of bmp genes in the interdigital regions. In this study we show that the duck interdigital web mesoderm exhibits an attenuated response to both BMP-induced apoptosis and TGFbeta-induced chondrogenesis in comparison with species with free digits. The attenuated response to these signals is accompanied by a reduced pattern of expression of msx-1 and msx-2 genes. Local application of FGF in the duck interdigit expands the domain of msx-2 expression but not the domain of msx-1 expression. This change in the expression of msx-2 is followed by a parallel increase in spontaneous and exogenous BMP-induced interdigital cell death, while the chondrogenic response to TGFbetas is unchanged. The regression of AER, as deduced by the pattern of extinction of fgf-8 expression, takes place in a similar fashion in the chick and duck regardless of the differences in interdigital cell death and msx gene expression. Implantation of BMP-beads in the distal limb mesoderm induces AER regression in both the chick and duck. This finding suggests an additional role for BMPs in the physiological regression of the AER. It is proposed that the formation of webbed vs free-digit feet in amniota results from a premature differentiation of the interdigital mesoderm into connective tissue caused by a reduced expression of msx genes in the developing autopod.

L2 ANSWER 86 OF 93 MEDLINE on STN DUPLICATE 22
ACCESSION NUMBER: 1998043861 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9334274
TITLE: A role for FGF-8 in the dorsoventral patterning of the zebrafish gastrula.
AUTHOR: Furthauer M; Thisse C; Thisse B
CORPORATE SOURCE: Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS, INSERM, ULP, Illkirch, France.
SOURCE: Development (Cambridge, England), (1997 Nov) Vol. 124, No. 21, pp. 4253-64.
Journal code: 8701744. ISSN: 0950-1991.
PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF034264
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 9 Jan 1998
Last Updated on STN: 3 Mar 2000
Entered Medline: 17 Dec 1997

AB Signals released from Spemann's organizer, together with ventralizing factors such as BMPs, are necessary to pattern the dorsoventral axis of the vertebrate embryo. We report that a member of the FGF family, fgf-8, not secreted by the axial mesoderm but expressed in a dorsoventral gradient at the margin of the zebrafish gastrula, also contributes to the establishment of the dorsoventral axis of the embryo. Ectopic expression of FGF-8 leads to the expansion of dorsolateral derivatives at the expense of ventral and posterior domains. Moreover, FGF-8 displays some organizer properties as it induces the formation of a partial secondary axis in the absence of factors released from Spemann's organizer territory. Analysis of its interaction with the ventralizing factors, BMPs, reveals that overexpression of FGF-8 inhibits the expression of these factors in the ventral part of the embryo as early as blastula stage, suggesting that FGF-8 acts upstream of BMP2 and BMP4. We conclude that FGF-8 is involved in defining dorsoventral identity and is an important organizing factor responsible for specification of mesodermal and ectodermal dorsolateral territories of the zebrafish gastrula.

L2 ANSWER 87 OF 93 MEDLINE on STN
ACCESSION NUMBER: 1998152849 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9493830
TITLE: Msx1 expressing mesoderm is important for the apical ectodermal ridge (AER)-signal transfer in chick limb development.
AUTHOR: Hara K; Ide H
CORPORATE SOURCE: Biological Institute, Graduate School of Science, Tohoku University, Aoba, Sendai, Japan.
SOURCE: Development, growth & differentiation, (1997 Dec) Vol. 39, No. 6, pp. 705-14.
Journal code: 0356504. ISSN: 0012-1592.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 22 Apr 1998
Last Updated on STN: 22 Apr 1998
Entered Medline: 14 Apr 1998

AB The apical ectodermal ridge (AER) is a specialized thickening of the distal limb ectoderm, and its signals are known to support limb morphogenesis. The expression of a homeobox gene, Msx1, in the distal limb mesoderm depends on signals from the AER. In the present paper it is reported that Msx1 expression in the distal mesoderm is necessary for the transfer of AER signals in chick limb buds. Interruption of AER-mesoderm interaction by insertion of a thick filter led to the inhibition of pattern specification in the mesoderm just under the filter. In such cases, the expression of Msx1 disappeared in the mesoderm under the filter, suggesting that AER is able to signal over short ranges. In advanced limb buds, Msx1 is also expressed in the proximal mesoderm under the anterior ectoderm. However, it was found that a grafted antero-proximal mesoderm shows no inhibitory effects on pattern specification of the host mesoderm, as is the case with the distal mesoderm. On the other hand, grafted mesoderms without potent Msx1 re-expression, even underneath AER, disturbed normal limb development. In

such cases, the expression of Msx1 disappeared in the mesoderm under the grafts, whereas Fgf-8 expression was maintained in the AER above the graft. These results indicate that the expression of Msx1 in the mesoderm is important for the transfer of AER signals.

L2 ANSWER 88 OF 93 MEDLINE on STN
ACCESSION NUMBER: 97446070 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9299117
TITLE: Limb initiation and development is normal in the absence of the mesonephros.
AUTHOR: Fernandez-Teran M; Piedra M E; Simandl B K; Fallon J F; Ros M A
CORPORATE SOURCE: Departamento de Anatomia y Biologia Celular, Universidad de Cantabria, Santander, 39011, Spain.
CONTRACT NUMBER: HD32551 (NICHD)
SOURCE: Developmental biology, (1997 Sep 15) Vol. 189, No. 2, pp. 246-55.
Journal code: 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 24 Oct 1997
Last Updated on STN: 24 Oct 1997
Entered Medline: 16 Oct 1997

AB With rapid progress in understanding the genes that control limb development and patterning interest is becoming focused on the factors that permit the emergence of the limb bud. The current hypothesis is that FGF-8 from the mesonephros induces limb initiation. To test this, the inductive interaction between the Wolffian duct and intermediate mesoderm was blocked rostral to the limb field, preventing mesonephric differentiation while maintaining the integrity of the limb field. The experimental outcome was monitored by following expression of cSim1 and Lmx1, molecular markers for the duct and the mesonephros, respectively. Evidence is presented that the intermediate mesoderm undergoes apoptosis when the inductive interaction with the Wolffian duct is blocked. fgf-8 expression was undetectable in the mesonephric area of embryos with confirmed absence of mesonephros; nevertheless, limb buds formed and limb development was normal. The mesonephros in general, and specifically its fgf-8 expression, was shown to be unnecessary for limb initiation and development; the hypothesis linking the mesonephros and limb development is not supported. Further studies of axial influences on limb initiation should now concentrate on medial structures such as Hensen's node and paraxial mesoderm; the alternative that no axial influences are required should also be examined.

L2 ANSWER 89 OF 93 MEDLINE on STN
ACCESSION NUMBER: 97415695 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9268570
TITLE: Hensen's node provides an endogenous limb-forming signal.
AUTHOR: Dealy C N
CORPORATE SOURCE: Department of Anatomy, University of Connecticut Health Center, Farmington, Connecticut 06030, USA.
CONTRACT NUMBER: HD22610 (NICHD)
SOURCE: Developmental biology, (1997 Aug 15) Vol. 188, No. 2, pp. 216-23.
Journal code: 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 13 Oct 1997
Last Updated on STN: 13 Oct 1997
Entered Medline: 1 Oct 1997

AB Acquisition of limb-forming ability by discrete regions of the lateral plate of the chick embryo is thought to depend on a signaling cascade moving sequentially from the area of Hensen's node to the somitic mesoderm, the intermediate mesoderm, and then to the prospective limb-forming regions of the lateral plate (Stephens et al., 1991). In the present study it is demonstrated that grafts of Hensen's node can induce the formation of supernumerary rudimentary limbs from the non-limb-forming flank region of the lateral plate of stage 9-15 chick embryos. The rudimentary limbs that form from the flank in response to Hensen's node grafts often contain elongated, jointed cartilaginous elements arranged in three distinct proximodistal segments resembling the developing stylopod, zeugopod, and autopod and express the limb-characteristic genes Msx-2 and BMP-4. However, the rudimentary limbs are incomplete and nonpolarized in that they do not form girdles or paired skeletal elements and fail to express sonic hedgehog, FGF-4, and FGF-8, signaling molecules that have been implicated in regulating the patterning of the developing limb bud. These results indicate that Hensen's node can provide a limb-forming signal to the lateral mesoderm, but that other signals are necessary to promote the expression of genes required for the complete patterning and morphogenesis of the limb.

L2 ANSWER 90 OF 93 EMBASE DUPLICATE 23

ACCESSION NUMBER: 96244650 EMBASE
DOCUMENT NUMBER: 1996244650
TITLE: The limb field mesoderm determines initial limb bud anteroposterior asymmetry and budding independent of sonic hedgehog or apical ectodermal gene expressions.
AUTHOR: Ros M.A.; Lopez-Martinez A.; Simandl B.K.; Rodriguez C.; Belmonte J.C.I.; Dahn R.; Fallon J.F.
CORPORATE SOURCE: Department of Anatomy, University of Wisconsin, 1300 University Avenue,Madison, WI 53706, United States
SOURCE: Development, (1996) Vol. 122, No. 8, pp. 2319-2330. .
ISSN: 0950-1991 CODEN: DEVPED
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 , Anatomy, Anthropology, Embryology and Histology
021 Developmental Biology and Teratology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Sep 1996
Last Updated on STN: 16 Sep 1996

AB We have analyzed the pattern of expression of several genes implicated in limb initiation and outgrowth using limbless chicken embryos. We demonstrate that the expressions of the apical ridge associated genes, Fgf-8, Fgf-4, Bmp-2 and Bmp-4 are undetectable in limbless limb bud ectoderm; however, FGF2 protein is present in the limb bud ectoderm. Shh expression is undetectable in limbless limb bud mesoderm. Nevertheless, limbless limb bud mesoderm shows polarization manifested by the asymmetric expression of Hoxd-11, -12 and -13, Wnt-5a and Bmp-4 genes. The posterior limbless limb bud mesoderm, although not actually expressing Shh, is competent to express it if supplied with exogenous FGF or transplanted to a normal apical ridge environment, providing further evidence of mesodermal asymmetry. Exogenous FGF applied to limbless limb buds permits further growth and determination of recognizable skeletal elements, without the development of an apical ridge. However, the cells competent to express Shh do so at reduced levels; nevertheless, Bmp-2 is then rapidly expressed in the posterior limbless mesoderm. limbless limb buds appear as bi-dorsal structures, as

the entire limb bud ectoderm expresses Wnt-7a, a marker for dorsal limb bud ectoderm; the ectoderm fails to express En-1, a marker of ventral ectoderm. As expected, C-Lmx1, which is downstream of Wnt-7a, is expressed in the entire limbless limb bud mesoderm. We conclude that anteroposterior polarity is established in the initial limb bud prior to Shh expression, apical ridge gene expression or dorsal-ventral asymmetry. We propose that the initial pattern of gene expressions in the emergent limb bud is established by axial influences on the limb field. These permit the bud to emerge with asymmetric gene expression before Shh and the apical ridge appear. We report that expression of Fgf-8 by the limb ectoderm is not required for the initiation of the limb bud. The gene expressions in the pre-ridge limb bud mesoderm, as in the limb bud itself, are unstable without stimulation from the apical ridge and the polarizing region (Shh) after budding is initiated. We propose that the defect in limbless limb buds is the lack of a dorsal-ventral interface in the limb bud ectoderm where the apical ridge induction signal would be received and an apical ridge formed. These observations provide evidence for the hypothesis that the dorsal-ventral ectoderm interface is a precondition for apical ridge formation.

L2 ANSWER 91 OF 93 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1997:87623 BIOSIS
DOCUMENT NUMBER: PREV199799379336
TITLE: Refined mapping of a gene for split hand-split foot malformation (SHFM3) on chromosome 10q25.
AUTHOR(S): Raas-Rothschild, A.; Manouvrier, S.; Gonzales, M.; Farriaux, J. P.; Lyonnet, S.; Munnich, A. [Reprint author]
CORPORATE SOURCE: Dep. Genetique, INSERM U-391, Hopital des Enfants-Malades, 149 rue de Sevres, 75743 Paris Cedex 15, France
SOURCE: Journal of Medical Genetics, (1996) Vol. 33, No. 12, pp. 996-1001.
CODEN: JMDGAE. ISSN: 0022-2593.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Feb 1997
Last Updated on STN: 26 Feb 1997

AB Split hand-split foot malformation (SHFM) is a genetically heterogeneous limb developmental defect characterised by the absence of digital rays and syndactyly of the remaining digits. Three disease loci have recently been mapped to chromosomes 7q21 (SHFM1), Xq26 (SHFM2), and 10q25 respectively (SHFM3). We report the mapping of SHFM3 to chromosome 10q25 in two large SHFM families of French ancestry (Zmax for the combined families=6.62 at theta = 0 for marker AFM249wc5 at locus D10S222). Two recombinant events reduced the critical region to a 9 cM interval (D10S1709-D10S1663) encompassing several candidate genes including a paired box gene PAX2 (Zmax = 5.35 at theta = 0). The fibroblast growth factor 8 (FGF 8), the retinol binding protein (RBP4), the zinc finger protein (ZNF32), and the homeobox genes HMX2 and HOX11 are also good candidates by both their position and their function.

L2 ANSWER 92 OF 93 MEDLINE on STN DUPLICATE 24

ACCESSION NUMBER: 96384724 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8792608
TITLE: Analysis of limb patterning in BMP-7-deficient mice.
AUTHOR: Hofmann C; Luo G; Balling R; Karsenty G
CORPORATE SOURCE: GSF, Forschungszentrum fur Umwelt und Gesundheit, Institut fur Saugetiergenetik, Neuherberg, Oberschleissheim-Munich, Germany.
SOURCE: Developmental genetics, (1996) Vol. 19, No. 1, pp. 43-50.
Journal code: 7909963. ISSN: 0192-253X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 27 Feb 1997
Last Updated on STN: 27 Feb 1997
Entered Medline: 11 Feb 1997

AB Bone morphogenetic proteins (BMPs) are polypeptide signaling molecules, belonging to the TGF-beta superfamily. They were originally identified by their ability to induce ectopic bone formation, but their expression patterns in embryos suggest multiple functions. BMP-7-deficient mice show among other mesodermal and skeletal patterning defects, polydactyly in the hindlimbs [Luo G, Hofmann C, Bronckers ALJJ, Sohocki M, Bradley A, Karsenty G (1995): Genes Dev 9:2808-2820; Dudley AT, Lyons KM, Robertson EJ (1995): Genes Dev 9:2795-2807]. Here we report a more detailed analysis of the limb phenotype in BMP-7-deficient mice using in situ hybridization to monitor expression of molecules implicated in patterning processes of the developing vertebrate limb. In previous studies we showed that Sonic hedgehog (Shh) was expressed normally, but Hoxd-13 expression in limb mesenchyme was lower in BMP-7 mutant limbs. Here we show that Hoxd-11 expression domains are also contracted and decreased in intensity in mutant limbs, suggesting that 5' genes of the Hoxd cluster are coordinately downregulated, while another Bmp, Bmp-2, which can be activated by Shh, is similarly expressed. The mutant limb buds are broader than normal buds, and fibroblast growth factor Fgf-8 is expressed throughout the extended ridge. However, expression of the homeobox gene Msx-1, which has been shown to be involved in epithelial-mesenchymal interactions during limb development, was decreased in the mesenchyme of BMP-7 mutant limbs. Taken together, our data suggest that BMP-7 is involved in regulating proliferation and/or epithelial-mesenchymal interactions in the developing limb.

L2 ANSWER 93 OF 93 MEDLINE on STN DUPLICATE 25
ACCESSION NUMBER: 96227537 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8645604
TITLE: Expression of bone morphogenetic protein-4 (BMP-4), bone morphogenetic protein-7 (BMP-7), fibroblast growth factor-8 (FGF-8) and sonic hedgehog (SHH) during branchial arch development in the chick.
AUTHOR: Wall N A; Hogan B L
CORPORATE SOURCE: Department of Cell Biology, Vanderbilt University Medical School, Nashville, TN 37232, USA.
CONTRACT NUMBER: CA48799 (NCI)
SOURCE: Mechanisms of development, (1995 Nov) Vol. 53, No. 3, pp. 383-92.
Journal code: 9101218. ISSN: 0925-4773.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 5 Aug 1996
Last Updated on STN: 5 Aug 1996
Entered Medline: 23 Jul 1996

AB Expression of Fgf-8, Bmp-4, Bmp-7, and shh in the branchial arches of the chick embryo is examined by in situ hybridization. Fgf-8 expression is initially broad and diffuse, becoming more tightly restricted, particularly in the epithelium of the posterior ectodermal margin (PEM) of the 2nd branchial arch. Bmp-7 transcripts, first seen at stage 12 in discrete regions corresponding to the developing branchial clefts, are later detected in both clefts and arches, including the PEM of the 2nd arch while Bmp-4 transcripts are detected at stage 18 in the distal tips of the arches. Shh expression remains localized, overlapping with both Bmp-7 and Fgf-8 in the PEM of the 2nd arch at stages 16 and 18. Based on these data, a

model is proposed for the role of these signalling molecules in branchial arch development.